

REMARKS

Applicants would first like to thank the Examiner for finding claim 114 allowable. Claims 41, 44, 49-52, 54-57, 59, 62, 64-66, 71, and 114 are currently pending in this application. Claim 41 has been amended to correct a typographical error and to differentiate between L₁ and L₂. Specifically, claim 41 was amended to recite that L₁ is a branched or unbranched, hydrophilic uncharged polymer selected from the group consisting of polyethylene glycol (PEG) and polysaccharides, and having a molecular weight less than about 2000 Daltons, and L₂ is a branched or unbranched, hydrophilic uncharged polymer selected from the group consisting of polyethylene glycol (PEG) and polysaccharides, and having a molecular weight of about 80 to about 4000 Daltons. Support for this amendment can be found in the specification as originally filed on page 16, lines 3-13. Claim 54 was amended to recite that L₁ or L₂ has a molecular weight of from about 100 to less than about 1500 Daltons. Support for this amendment can be found in the specification as originally filed on page 16, lines 3-13. No new matter has been introduced into this application by any of the amendments.

I. The Rejections Under 35 U.S.C. § 102(b) Should Be Withdrawn

Claims 41, 44, 49-52, 64-66, and 71 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 5,876,946 to Burbaum *et al.* ("Burbaum").

Claims 41, 44, 49-51, 60, 54-57, and 71 were also rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Polymeric Materials Science and Engineering, 1998, 79:471-472 to Belcheva *et al.* ("Belcheva").

Applicants respectfully traverse each of these rejections for the reasons set forth herein.

Anticipation is established under 35 U.S.C. § 102(b) when a single prior art reference, published more than one year prior to the earliest applicable priority date of the subject patent, discloses, expressly or under principles of inherency, each and every element of a claimed invention. *EMI Group N. Am. v. Cypress Semiconductor*, 268 F.3d 1342, 1350 (Fed.

Cir. 2001); *Telemac Cellular Corp. v. Topp Telecom Inc.*, 247 F.3d 1316, 1327 (Fed. Cir. 2001); *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365 (Fed. Cir. 1999); *Glaverbel Societe Anonyme v. Northlake Mktg. & Supply*, 45 F.3d 1550, 1554 (Fed. Cir. 1995). It is settled law that a prior art reference must disclose all of the elements of a claim in order to anticipate the invention recited by that claim. *See Manual of Patent Examining Procedure* § 2131. There must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. *See Scripps Clinic & Research Fdn. v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).

A. The Anticipation Rejection Over Burbaum Should Be Withdrawn

According to the Office Action, Burbaum discloses a library of peptidic substrates. The peptidic substrates comprise a peptide (Ps) coupled to a kinase domain affixed to a polymer bead and labeled with Cy5. The Office Action states that the peptide comprises “end” residues with different net charges and the polymer bead includes polyethylene glycol (PEG)-grafted polystyrene beads. The label includes other fluorescent labels such as Texas red and chemiluminescent labels. According to the Office Action, the peptidic substrate of Burbaum correspond to the claimed peptidic substrate member with the general formula of $*F-R_1-L_1-R_2-P_{Hc1}-P_s-P_{Hc2}-(R_3-L_2-R_4-T)_y$, wherein y is 0, L_1 is polyethylene glycol (PEG), R_1 is a covalent bond consisting of a nitrogen heteroatom, and R_2 is a covalent bond consisting of an oxygen heteroatom, P_{Hc1} is a lysine, (*i.e.*, in the formula of $P_{Hc1} = A_c(A_H)_nA_m$, A_c = lysine, A_m = covalent bond, and since $n = 0$, A_H is 0), and P_{Hc2} is a covalent bond with a carboxylic acid moiety, *i.e.* in the formula of $P_{Hc2} = A_m(A_H)_nA_c$: A_c = carboxylic acid moieties since $y = 0$, A_m = covalent bond, and since $n = 0$, A_H is 0. Thus the Examiner alleges that the library of Burbaum anticipates the presently claimed library. Applicants respectfully traverse this rejection.

The pending claims are directed a library of water-soluble peptidic substrates. Applicants have amended claim 41 to recite that L_1 is a branched or unbranched, water-soluble uncharged polymer selected from the group consisting of polyethylene glycol (PEG) and polysaccharides, and having a molecular weight less than about 2000 Daltons. In

contrast, the assay of Burbaum utilizes binding of a label to suspendable cells or to suspendable solid supports, which are by definition insoluble. The Examiner has alleged that the recitation of the phrase "water-soluble" has not been given patentable weight because it occurs in the preamble. Applicants respectfully submit that in view of the claim amendment, the Examiner should withdrawal the rejection under 35 U.S.C. § 102(b).

B. The Anticipation Rejection Over Belcheva Should Be Withdrawn

According to the Office Action, Belcheva discloses water-soluble fluorescein polymer-peptide conjugates. The Office Action alleges that the peptide (Ps) is 5 amino acids in length; the polymer is polyethylene glycol (PEG) with a MW of either 2000 or 5000; and the water-soluble fluorescein polymer-peptide conjugates of Belcheva (*i.e.*, GRGDY-PEG-fluorescein) correspond to the claimed substrate member with the general formula of *F-R₁-L₁-R₂-P_{Hc1}-P_s-P_{Hc2}-(R₃-L₂-R₄-T)_y, wherein y is 0 (refers to claims 41 and 71), *F is fluorescein (refers to instant claims 49-51), L₁ is polyethylene glycol (PEG), R₁ and R₂ are each a covalent bond, P_{Hc1} is a covalent bond (*i.e.*, in the formula of P_{Hc1} = A_c(A_H)_nA_m: A, and A_m = covalent bond, and since n = 0, A_H is 0), and P_{Hc2} is a covalent bond with a carboxylic acid moiety, (*i.e.*, in the formula of P_{Hc2} = A_m(A_H)_nA_c: A_c = carboxylic acid moieties since y = 0, A_m = covalent bond, and since n = 0, A_H is 0). Thus according to the Office Action, the water-soluble fluorescein polymer-peptide conjugates of Belcheva anticipate the presently claimed library. Applicants respectfully traverse this rejection.

Applicants have amended claim 41 to recite that L₁ is a branched or unbranched, hydrophilic uncharged polymer selected from the group consisting of polyethylene glycol (PEG) and polysaccharides, and having a molecular weight less than about 2000 Daltons, and L₂ is a branched or unbranched, hydrophilic uncharged polymer selected from the group consisting of polyethylene glycol (PEG) and polysaccharides, and having a molecular weight of about 80 to about 4000 Daltons. Belcheva in contrast discloses PEG of molecular weight of 2000-5000. Because Belcheva does not disclose all of the elements of the pending claims, the reference cannot anticipate the claims. *EMI Group N. Am. v. Cypress Semiconductor*.

Applicants respectfully submit that in view of the claim amendment, the Examiner should withdrawal the rejection under 35 U.S.C. § 102(b).

II. The Rejection Under 35 U.S.C. § 103(a) Should be Withdrawn

Claims 41, 44, 49-52, 54-57, 59, 62, 64-66, and 71 were rejected on pages 7-9 of the Office Action under 35 U.S.C. § 103(a) as allegedly obvious over Belcheva and Pomroy *et al.*, *Biochemical and Biophysical Research Communications*, 1998, 245(2), 618-621 (“Pomroy”).

The Federal Circuit has set forth three basic criteria that must be met to establish a case of *prima facie* obviousness. First, there must have been at the time of the invention a motivation to combine or modify the teachings of the references cited. *Ecolchem, Inc. v. Southern California Edison Company*, 227 F.3d 1361, 1372 (Fed. Cir. 2000) (holding obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination); *see also In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988) (holding that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art). Second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious. *In re Royka*, 490 F.2d 488 (CCPA 1974) (holding that to establish *prima facie* obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art); *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991) (holding that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant’s disclosure). Third, there must have been at the time of the invention a reasonable expectation of success. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-1208 (Fed. Cir. 1991), *cert. denied* 502 U.S. 856 (1991) (holding that obviousness requires references to show that there was, at the time of the invention, a reasonable expectation of success).

**A. The Rejections Over Belcheva and Pomroy Under
35 U.S.C. § 103(a) Should be Withdrawn**

According to the Office Action, it was alleged that it would have been obvious to a person of ordinary skill in the art at the time the invention was made to include in the water-soluble fluorescein polymer-peptide conjugates - a thioether linkage at the R₂ position and the “end” residues (*i.e.*, P_{Hc1} and P_{Hc2}) of the peptide having a different net charge as taught by Pomroy when used in the library of Belcheva. The Office Action further alleges that one of ordinary skill in the art would have been motivated to couple the peptide to the polyethylene glycol (PEG) by way of the cysteine and the “end” residues (*i.e.*, P_{Hc1} and P_{Hc2}) of the peptide having a different net charges in the water-soluble fluorescein polymer-peptide conjugates of Belcheva for the advantage of providing a cleavable disulfide bond between the thiol-reactive PEG and the protein because both Belcheva and Pomroy disclose a composition wherein the peptide is coupled to the polyethylene glycol. Furthermore, the Office Action alleges that one of ordinary skill in the art would have a reasonable expectation of success in the combination of Belcheva and Pomroy because Pomroy discloses the success of PEGylation of the peptide using PEG-a-Cys reagent. Applicants respectfully traverse this rejection.

Applicants have amended claim 41 to recite that L₁ is a branched or unbranched, hydrophilic uncharged polymer selected from the group consisting of polyethylene glycol (PEG) and polysaccharides, and having a molecular weight less than about 2000 Daltons, and L₂ is a branched or unbranched, hydrophilic uncharged polymer selected from the group consisting of polyethylene glycol (PEG) and polysaccharides, and having a molecular weight of about 80 to about 4000 Daltons. Because Belcheva and Pomroy do not disclose or suggest all of the elements of the pending claims, the claims cannot be obvious in view of these references. As the Examiner is aware, it is the invention as a whole that must be considered in obviousness considerations not bits and pieces of various references. *Hartness International, Inc. v. Simplimatic Engineering Co.*, 819 F.2d 1100 (Fed. Cir. 1987). In view of the claim amendments, Applicants submit that the legally required *prima facie* case of obviousness based on the disclosures of Belcheva and Pomroy is not present.

For the above reasons, Applicants respectfully request that the Examiner withdrawal the rejection under 35 U.S.C. § 103.

III. Conclusion

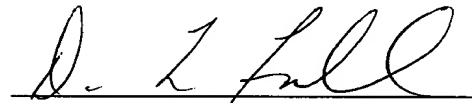
Respectfully, Applicants submit that the rejections to the claims in the application should be withdrawn based on the amendments and remarks made herein. Favorable consideration and a Notice of Allowance are earnestly solicited.

Except for issues payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310.

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